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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/993,842	11/05/2001	Dhiren R. Thakker	421/15/2	1627

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EXAMINER
MORAN, MARJORIE A

ART UNIT	PAPER NUMBER
1631	3

DATE MAILED: 07/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/993,842	THAKKER ET AL.	
	Examin r	Art Unit	
	Marjorie A. Moran	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 November 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 7-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 7-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 7-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the phrase "characterized as having" with respect to enzymatic activity. Enzymes typically display activity with respect to substrates, or participate in or catalyze reactions, but do not commonly comprise or "have" reactions as an inherent characteristic. As it is therefore unclear what is meant by the phrase "characterized as having", the claim is indefinite. See suggestions below.

Claim 1 recites the phrase "associated with the metabolic activity" of an enzyme with respect to a reaction. It is unclear what limitation applicant intends by this phrase; e.g. coupled to a general metabolic process, coupled to another reaction in which the enzyme participates, resulting from a previous enzymatic reaction, etc., therefore this phrase renders the claim indefinite. To overcome the two rejections with regard to claim 1, the examiner recommends rewriting the claim to recite definite limitations; e.g. Replacing "the enzyme characterized by ..." in lines 4-7 with --wherein the enzyme participates in a side reaction, thereby producing a chemical species which then reacts with the indicator precursor compounds--.

Claim 1 recites an indicator compound produced by reaction with a chemical species. It is unclear if this limitation is intended as a method step, or is intended to limit

the indicator compound, therefore the claim is indefinite. Applicant should note that a "method of producing" is not a structural or functional limitation of a compound. If applicant intends to limit the indicator to be one produced by reaction of a precursor with a chemical species, then a separate step of producing such an indicator compound, or of reacting the precursor with the chemical species, or a both, should be recited in the claim.

Claim 7 recites the phrase "associated with metabolic activity" in line 2. It is unclear what limitation applicant intends for this phrase, as set forth above, therefore use of the phrase renders the claim indefinite. This rejection may be overcome by deleting the phrase "associated with metabolic activity" in line 2.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 7 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by NAKANISHI *et al.* (US 4,341,868), as supported by OTA *et al.* (5,843,969).

NAKANISHI teaches a method of determining substrates (identifying or screening compounds for susceptibility to) xanthine oxidase wherein the compound is reacted with the enzyme such that hydrogen peroxide is formed, then the hydrogen

peroxide measured by detecting absorbance changes; i.e. colorimetrically (col. 1, lines 25-47 and col. 5, line 54-col. 6, line 22). OTA provides support that hydrogen peroxide produced by metabolism of a substrate by xanthine oxidase is produced as a result of a secondary or "side" reaction (col. 1, lines 38-46), therefore claims 1, 7 and 8 are anticipated.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 7-8 and 10 rejected under 35 U.S.C. 103(a) as being unpatentable over NAKANISHI *et al.* (US 4,341,868), as supported by OTA *et al.* (US 5,843,969).

Claim 1 recites a method of screening a candidate compound for susceptibility to metabolism by xanthine oxidase (i.e. identifying a substrate for xanthine oxidase) by reacting the candidate compound, the enzyme, and an indicator compound precursor are reacted, wherein enzymatic activity produces a chemical which reacts with the indicator precursor to produce an indicator, then detecting the indicator compound produced, wherein detection the indicator indicates that the candidate compound is a substrate of the enzyme. Claim 7 limits the chemical produced by enzymatic activity to be a reactive oxygen species. Claim 8 limits the indicator precursor to be a fluorogenic, colorimetric, or chemiluminescent compound, or a combination of these. Claim 10 limits the method to screen a plurality of candidate compounds simultaneously.

NAKANISHI teaches a method for determining substrates of xanthine oxidase wherein hydrogen peroxide is produced by the oxidase and measured colorimetrically, as set forth above. NAKANISHI teaches screening of a plurality of compounds in his method (col. 6, Table 1), but does not specifically teach simultaneous screening.

It would have been obvious to one of ordinary skill in the art at the time of invention to have simultaneously screened the plurality of compounds as xanthine oxidase substrates in the method of NAKANISHI where the motivation would have been to facilitate comparison of results and to save time by running the method for several compounds at the same time rather than sequentially, as suggested by the Heat Stability experiments of NAKANISHI (col. 6, lines 24-29). No criticality or unexpected result has been shown for simultaneous screening of compounds in the method. For these reasons, claims 1, 6-8 and 10 are obvious.

Claims 9 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over NAKANISHI *et al.* (US 4,341,868) and OTA *et al.* (5,843,969) as applied to claims 1 and 10 above, and further in view of CHRZANOWSKA-LIGHTOWLERS *et al.* (Analytical Biochem. (1993) vol. 214, pages 45-49).

The claims recite a method for screening for substrate of xanthine oxidase, as set forth above. Claims 9 and 11 limit the method to one performed in at least one, or in multiple wells of a multi-well plate.

NAKANISHI teaches a method for screening for an enzyme substrate, and makes obvious simultaneous screening of a plurality of compounds, as set forth above. NAKANISHI does not teach performing his method on a multi-well plate.

CHRZANOWSKA-LIGHTOWLERS teaches an assay for detecting oxidase activity which is performed on a microtiter (multi-well) plate (p. 45, first paragraph).

It would have been obvious to one of ordinary skill in the art at the time of invention to perform the method of NAKANISHI in a multi-well plate, as suggested by the microtiter plate assay of CHRZANOWSKA-LIGHTOWLERS, where the motivation would have been to facilitate screening of multiple compounds in the method, as taught and suggested by NAKANISHI. No criticality or unexpected result has been shown for performing the method in a multi-well plate over performing the method in a plurality of any other type of container (e.g. individual test tubes). One skilled in the art would reasonably have expected success in performing the method of NAKANISHI in a multi-well plate because methods of performing various reactions and detecting indicator compounds resulting from those reactions in micro-well plates are well known in the art, and a method of detecting the results of oxidase reactions in micro-well plates, in particular, is taught by CHRZANOWSKA-LIGHTOWLERS. For these reasons, claims 9 and 11 are obvious.

Conclusion

Claims 1 and 7-11 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (703) 305-2363. The examiner can normally be reached on Monday to Friday, 7:30 am to 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (703) 308-4028. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 872-9306 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-3524.

MARJORIE MORAN
PATENT EXAMINER
Marjorie A. Moran

mam
July 11, 2003